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THE CULTIVATION OF THE BACILLUS LEPRAE.

E.R. ROST

THE INDIAN MEDICAL GAZETTE,
1904, 39.



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year 1894 by Lieutenant-Colonel Comins is significant:—"An increase in the ration of vegetable acids and vegetables has often little or no effect on this state, whereas the too marked acidity of the food is distasteful to the prisoners, and the appetite for the food is lessened. It is stated that a connexion can be traced between increased ration of vegetable acids and tendency to indigestion, diarrhoea and even dysentery." I should now add stomatitis also.

My observations during the present year have brought the following facts to light:—

1. That stomatitis in the jails may occur even in persons without any malarial taint in their systems.
2. That it is intimately connected with indigestion, particularly of an acid fermentative kind.
3. That neither fresh vegetables in excess nor meat diet is called for to rectify the condition which produces it.
4. That it can be effectually prevented by carefully eliminating the acid element from the food of the prisoners during the months of June, July and August, and by general improvement of the digestive function by the use of stomachics and digestives, of which capsicum and papaya are the handiest and most easily procurable.
5. That this disease in this district at any rate is entirely confined to the jail. I have vainly looked for it outside among the dispensary patients and the general population in the town as well as in the district.
6. That it occurs only during the rainy months of the year, namely, June, July, August and September, seldom occurring before and disappearing as soon as the cold weather sets in.
7. That it has a strange connection with dysentery incidence in the jail, both these diseases showing a tendency to increase and decrease in an inverse ratio to each other every month, as the following statement will show:—

Months of the year.	Number of dysentery cases.	Number of cases of ulceration of mouth.
January	...	...
February	...	...
March	4	...
April	2	...
May	5	...
June	8	23
July	12	12
August	8	23
September	4	1
October	...	7
November	2	...
December	3	...

In conclusion, it seems to me quite possible that jail dysentery and jail stomatitis may arise from one and the same cause, namely, irritation of the mucous membrane of the alimentary canal by an acid acid substance, the product of fermentative dyspepsia due indirectly to unaccustomed food and directly to excess of the acid element in the same, the result of this irritation manifesting itself as stomatitis in the mouth and as dysentery in the bowels.*

THE CULTIVATION OF THE BACILLUS LEPRÆ.

BY E. R. ROST,

CAPTAIN, I.M.S.,

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JUST as there is a class of bacteria which may be classified as anærobic, so is there a class of bacteria which may be classified as a-chloretic.

This class of bacteria is the acid-fast group, of which B. Tuberculosis, B. Lepræ, and B. of Lustgarten are pathogenic.

This conclusion was arrived at after extensive experiments based on a certain law of the periodicity of the pathogenic organisms, which has, however, not yet been published, but which is based on the law of the periodicity of the atomic weights of Mendeleïf.

I showed this theory to some authorities when in England last June, but it was thought to be rather far fetched, it was not until returning to Burma last August that I commenced to practically investigate the truth of the theory, and this led to the cultivation of the acid-fast series and the manufacture of a leprolin on the lines of Koch's tuberculin, which has given very encouraging results when injected into lepers.

Although these experiments are far from being completed, I hasten to lay before you the facts as far as I have yet gone, as the importance of the discovery justifies its being universally known as soon as possible in order that those more competent than myself may further investigate the subject, for the benefit of those unfortunate beings affected with the terrible disease leprosy.

In this account I will refrain from theorizing, and will therefore not mention anything about this law of the periodicity of pathogenic organisms. Believing that the acid-fast series of Bacteria would not grow in the presence of salts of chlorine, I tried to extract the chlorides out of nutrient media, and this was first done by

* We commend this paper to the attention of Civil Surgeons in charge of Jails. This question of spongy gums is often coming up, and in many places these cases are regarded as scurvy or "incipient" scurvy. We invite discussion.—
ED., I. M. G.

making a medium from distilling beef extract which gave a clear fluid, which smelt strongly of beef. In this medium it was found that the *B. Tuberculosis* grew with great rapidity, and this led me to try to grow the *B. Lepræ* and the *B. of Lustgarten* in this medium. The leprosy bacillus was obtained from the fresh granulating sores of a case of leprosy, and that of Lustgarten from underneath a primary syphilitic sore, both these cultivations appeared on the second day, as white, stringy, streaky, heavy, deposits at the bottom of the tubes, which were difficult to shake up, but when shaken up formed a curly white, stringy filament in the tube. This on microscopic examination was found to give all the characteristic appearances of the *Bacillus Lepræ*, and was very resistant to acid, more so than the *Bacillus of Tubercle*.

They appeared as small beady bacilli of irregular size, which in fresh specimens were motile, they were straight and some had thicker ends than others, the beads appeared to be spores, as sometimes only the small round red stained balls were to be seen, and at other times the small spores as well as the bacilli, they grew in groups and sometimes were so massed together as to appear as a red mass. At times they appeared in long threads, like the tubercle bacillus appears sometimes in culture.

Numerous attempts to grow the bacillus in solid media, evidently due to the large amount of salts in agar, led me to adopt a further method of preparing the medium, and this was done by dialysis. By dialysing the nutrient agar through an animal membrane in hot distilled water for some days, I obtained a medium which was entirely free from salts, and in this I have grown the bacillus with the greatest ease. The bacillus of leprosy grows on the surface of solid media as a white or very slightly yellow beady growth, and the growth appears after two days' incubation at 37°C. like with the liquid medium. The bacillus had the same characteristics in the stained preparations taken from these cultures.

In dialysed beef broth or dialysed fish broth the bacillus grew also with the greatest ease, as did also the *Bacillus of Lustgarten* and the *Tubercle Bacillus*.

The appearance of the cultures of these three organisms is very similar, but the cultivations of leprosy were not so easily shaken up from the bottom of the tubes as the cultivations of tubercle, and those of the *Bacillus of Lustgarten* appeared to stick firmer than the others to the bottom of the tubes.

It was moreover found that glycerine is not at all necessary for the growth of these bacteria, and that in the case of leprosy it appears to prevent the growth altogether, moreover the specimens taken for observation are very hard to dry if there is any glycerine present.

It was found that the salts of iodine and bromine did not inhibit these bacteria, even

when in as large amount as 10 per cent., and the iodine and bromine became precipitated after some days in the tubes. But there appeared to be some choice for these halogens between these bacteria, for it was found that the *B. Tuberculosis* preferred the bromine salts and the *B. Lepræ* the iodine salts, though they did not grow in this media with the rapidity with which they grew in the plain media.

Over three hundred cultivations have been made of these bacteria in these media, and in no case has there been any reason to doubt that the organisms cultivated were not the *B. Lepræ*, the *B. Tuberculosis*, and the *B. of Lustgarten*, the cultivations of leprosy were obtained from several different cases of leprosy, after finding the bacillus in the granulations.

It was further found that the bacillus of leprosy sediments to 1 in 40 dilution with distilled water with the serum of cases of leprosy.

The next thing that was attempted was the manufacture of a leprolin on the lines of the manufacture of tuberculin laid down by Professor Koch.

Cultivations of leprosy in the distilled beef extract, which was further improved by the passage of superheated steam over the boiling extract, were allowed to grow at a temperature of 37°C. for six weeks, and then sterilised and passed through a Pasteur filter, and then glycerine added to the clear fluid. The injection of this into cases of leprosy has given very encouraging results, though it is too early yet to say with what benefit, the action of the leprolin is so marked that I am not waiting to see what is going to happen before publishing observations that I am now making, as it is necessary that others should try what has already been attained before going deeper into these experiments.

THE EFFECT OF THE INJECTION OF LEPROLIN INTO LEPERS.

Eleven cases of leprosy have now been injected with the material, the manufacture of which has been described above, and the action in these cases has been so marked and in some cases the improvement so obvious that it appears that there is something in this material, and certainly that its action is very similar to that of tuberculin in cases of tuberculosis.

The first case, a Chinaman, with anæsthetic leprosy and markings on the face and tubercles in the ears, was injected with 5 c.c. of the leprolin intra-muscularly in the buttock, there was only a slight reaction, the temperature rising to 99 F. and the pulse to 112, but the anæsthetic patches became slightly red and hot, and the patient said that he felt hot and light all over. The next day an injection of 20 c.c. was given in the other buttock, and the effect of this was almost instantaneous, as the pulse

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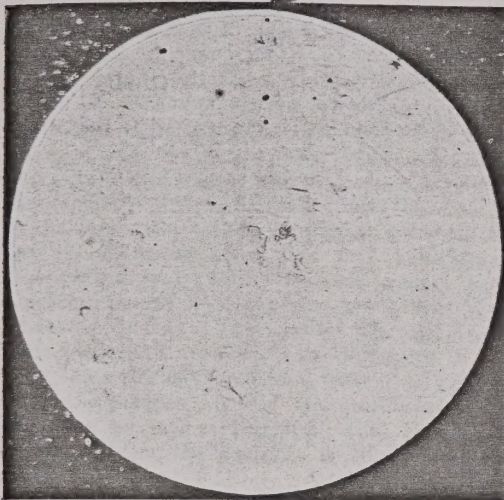


FIG. 1.—MICRO-PHOTOGRAPH OF STAINED SPECIMEN OF THE BACILLUS OF LEPROSY? FROM A CULTURE IN THE LIQUID MEDIUM.

Oil immersion $1/12$ in.

(Shows the beady appearance of the bacilli.)

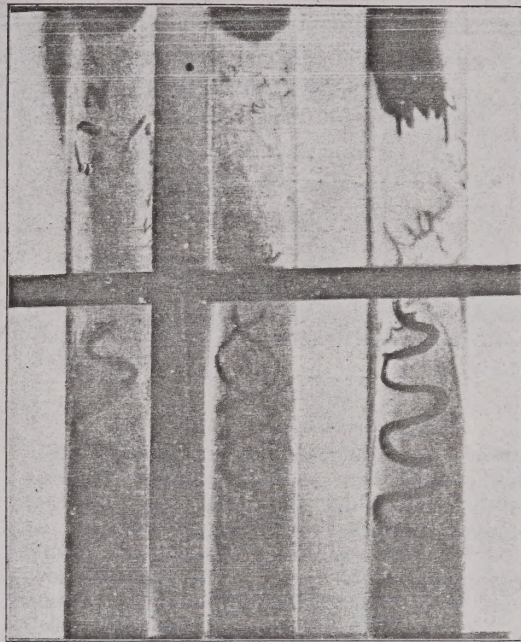


FIG. 3.—PHOTOGRAPH OF CULTURES OF THE LEPROSY BACILLUS ON SOLID MEDIUM? MADE FROM DIALYSED FISH EXTRACT AGAR.

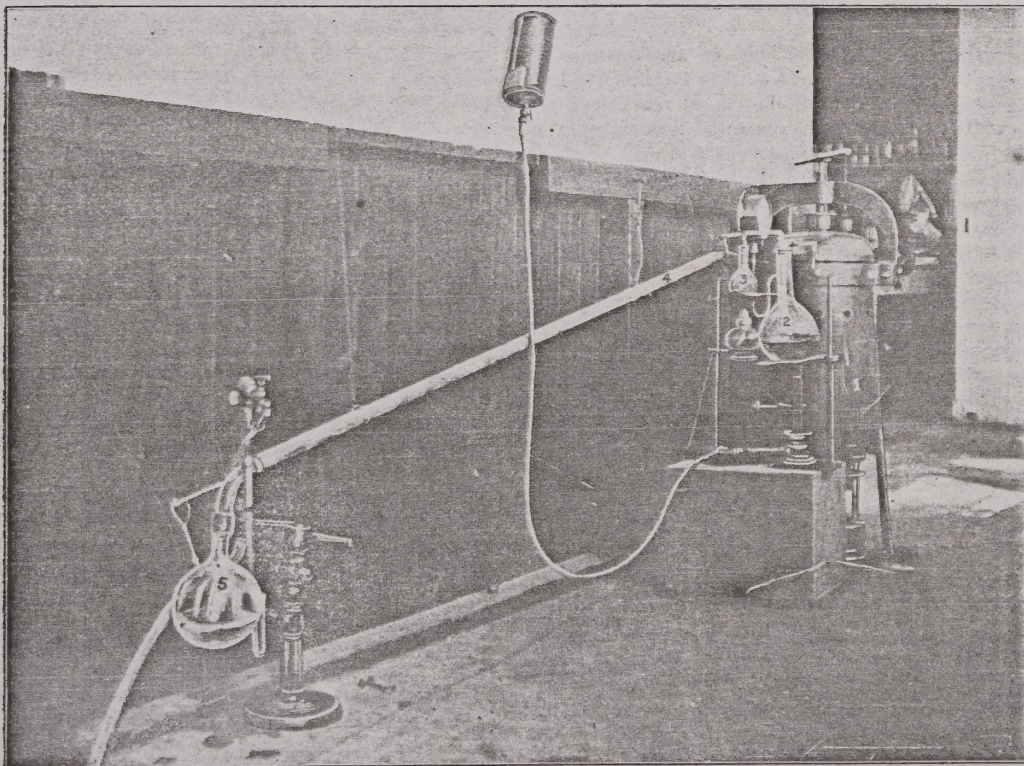


FIG. 2.—PHOTOGRAPH OF THE APPARATUS PREPARED FOR THE MANUFACTURE OF THE LIQUID DISTILLED MEDIUM.

(1. Autoclave. 2. Flask in which the beef extract is being boiled. 3. Catch flask, in case any boiling over occurs. 4. Condensing tube. 5. flask for catching the medium sterilized before.)

immediately rose to 110, the anæsthetic patches became red and hot, the breathing rapid, and the temperature rose to 101 F. The next day the sensation on the patches on the cheeks returned, the redness subsided, and the temperature fell between 100 and 99 F., and the pulse and respiration to normal.

Ten days after this another injection was given of the same amount, with similar results, the temperature going up to 100·5 four hours after, and the redness of the patches appearing only five minutes after the injection, it is now 20 days since he was first injected, and the nodules in the ears have become much less evident, the patches of anæsthesia on the face have almost disappeared, and there is now some slight sensation in the legs, whereas there was none whatever before. The patient has also been taking salt and applying salt ointment to the body, and the salt ointment should be applied when the patches are red and swollen after the injection, as it is at this time that the action of the salt on the bacteria is likely to take effect.

Ten other cases have been injected mostly at the Leper Asylum at Kemmendine, cases in all stages of the disease, and the reaction in nearly all these cases has been the same as that described above. The sensation returned in portions of the anæsthetic patches in some of these cases, one case showed signs of the breaking down of a nodule, which gave out some sanious fluid the day after, but which dried up again. In two cases there was no reaction noticeable after the injection; these cases had no ulceration and were early cases of the disease, and one case stated that he did not notice anything after the injection. The other cases said that they felt lighter in their legs and better after the injection, and certainly there has been a return of sensation most marked in some cases. A second injection has just been given to these cases, which, as before, was followed by a sharp rise of temperature to between 103 and 105, the injection was, as before, given in the buttock, and 20 c.c. of leprolin freshly prepared and from a somewhat better culture than before. There was a good deal of local swelling and redness of the affected parts, and the same symptoms as mentioned above.

These cases cannot be published in full until their after-history is known, I merely briefly state the symptoms to show that the action of this material is similar to that of tuberculin in consumption.

That the material injected was actually the toxins from cultivations of the leprosy bacillus there can appear little doubt, and that this material has an action in the disease, there can also be little doubt, but whether this action is beneficial or not time can alone show.

I shall be glad to forward cultures of the bacillus, or the leprolin, to anyone who would like to try its action.

"A CONTRIBUTION TO THE STUDY OF THE ACTION OF INDIAN COBRA POISON."*

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ON special duty for Snake Venom Research, under the orders of the Secretary of State for India. Communicated by Professor Sir THOMAS R. FRASER, F.R.S., Received January 18,—Read February 25, 1904. **

(Abstract.)

Previous Work on the Subject.

Brunton and Fayrer† discussed the pharmacology of cobra venom at some length; they attributed the effects of the poison to its action on the cerebro-spinal nerve-centres, especially on the respiratory centre. They observed that cobra venom had a direct action on cardiac muscle, and that it also affected the heart through the vagal system, but they did not lay much stress on circulatory failure. They surmised that the high and maintained blood-pressure of a cobraised animal was due to arteriolar constriction, but did not attempt to explain how this was brought about. Amongst the many other points of interest they took up, was the influence of artificial respiration in cobraism.

Cunningham in the 'Scientific Memoirs by Medical Officers of the Army in India'‡ urged the opposing theory that cobra venom acted on respiration through the blood and not through the nervous system.

Weir Mitchell and Reichert§ carried on Brunton and Fayrer's views. Their paper was mainly concerned with the venoms of other snakes than the cobra. They thought two factors were at work on the rate of the heart, viz., an increased activity of the accelerator centres, quickening the beat, and a direct action on the heart slowing it. They attributed the primary fall in blood-pressure to depression of the vaso-motor centres, but thought it might be partly cardiac. The rise they considered "capillary" and the final fall cardiac.

Bagotzi|| laid great stress on the rôle played by nerve-end paralyses (especially phrenic), and disputed Brunton's views that respiration was attacked through the medullary centre. He

* Read before the Royal Society, and sent by the Society for publication.

** Owing to the kindness of Professor Sir Thomas Fraser and of Professor E. A. Schäfer, the writer was enabled to carry out this research in the Pharmacological and Physiological Laboratories of the University of Edinburgh. Towards the expense of this research, grants were received from the British Medical Association and from the Moray Fund for the Endowment of Research (Edinburgh).

† Roy. Soc. Proc., vols. 21, 22 and 23.

‡ 1895, Part IX, and 1898, Part XI.

§ Smithsonian Contributions to Knowledge, 1890.

|| Virchow's 'Archiv für Path.', vol. 122, p. 201.



